

=> d his

(FILE 'USPAT' ENTERED AT 17:34:30 ON 14 JAN 97)

L1	1904 S (TUMOR NECROSIS FACTOR) OR TNF OR CACHECTIN
L2	251 S L1(P)RECEPTOR
L3	40 S L1(P)BINDING PROTEIN
L4	33 S L1(10A) ((BINDING PROTEIN) OR BP)
L5	157 S L1(P)INHIBITOR
L6	13 S L2(P)INHIBITOR

BEST AVAILABLE COPY

1. 5,582,998, Dec. 10, 1996, Monoclonal antibodies against human ****TNF****-****binding**** ****protein**** I (****TNF****-****BP**** I) and immunoassays therefor; G unther Adolf, 435/7.1, 7.92, 7.94, 70.21, 240.27; 436/811, 815; 530/388.1 [IMAGE AVAILABLE]
2. 5,525,626, Jun. 11, 1996, Treating susceptible human malignant tumors with 7-hydroxy-1,2-benzopyrone; Douglas R. Thornes, et al., 514/457; 424/649; 514/171, 274 [IMAGE AVAILABLE]
3. 5,519,119, May 21, 1996, Muteins of TNF pharmaceutical compositions and a method of making; Nobutoshi Yamada, et al., 530/351; 53/395, 402; 435/69.1, 69.5, 69.7, 252.3, 252.33, 320.1 [IMAGE AVAILABLE]
4. 5,512,544, Apr. 30, 1996, Pharmaceutical compositions comprising an anticytokine; David Wallach, et al., 514/12, 21; 530/350 [IMAGE AVAILABLE]
5. 5,478,925, Dec. 26, 1995, Multimers of the soluble forms of TNF receptors, their preparation and pharmaceutical compositions containing them; David Wallach, et al., 530/351; 424/85.1, 158.1, 450 [IMAGE AVAILABLE]
6. 5,476,774, Dec. 19, 1995, Quantitation of nucleic acids using the polymerase chain reaction; Alice M. Wang, et al., 435/91.2, 6, 320.1; 536/24.33; 935/77, 78 [IMAGE AVAILABLE]
7. 5,470,829, Nov. 28, 1995, Pharmaceutical preparation; Per Prisell, et al., 514/12; 424/85.1; 514/2, 8, 21; 525/54.1 [IMAGE AVAILABLE]
8. 5,464,820, Nov. 7, 1995, Specific inhibitors of tissue kallikrein; James Burton, et al., 514/16, 17, 18; 530/329, 331 [IMAGE AVAILABLE]
9. 5,426,181, Jun. 20, 1995, DNA encoding cytokine-induced protein, TSG-14; Tae H. Lee, et al., 536/23.5; 435/69.1, 252.3, 320.1; 536/23.1 [IMAGE AVAILABLE]
10. 5,395,760, Mar. 7, 1995, DNA encoding tumor necrosis factor-.alpha. and -.beta. receptors; Craig A. Smith, et al., 435/240.1; 424/85.1; 435/69.4, 172.3; 530/351, 388.23; 536/23.51 [IMAGE AVAILABLE] *Id May 10, 1990*
11. 5,359,039, Oct. 25, 1994, Isolated poxvirus A53R-equivalent tumor necrosis factor antagonists; Craig A. Smith, et al., 530/350; 424/186.1, 232.1; 530/826; 536/23.72; 930/220 [IMAGE AVAILABLE]
12. 5,359,037, Oct. 25, 1994, Antibodies to ****TNF**** ****binding**** ****protein**** I; David Wallach, et al., 530/388.22; 424/143.1, 172.1; 530/388.1, 389.1 [IMAGE AVAILABLE]
13. 5,344,915, Sep. 6, 1994, Proteins and the preparation thereof;

4 Hans-Georg LeMaire, et al., 530/350, 395, 413, 416 [IMAGE AVAILABLE]

14. 5,324,655, Jun. 28, 1994, Human Y-interferon signal peptide-tumor necrosis factor(TNF) gene fusions; Michael Kriegler, et al., 435/240.2, 69.1, 69.5, 69.7, 69.8, 172.1, 172.3, 240.1, 320.1; 536/23.1, 23.2, 23.4, 23.5, 23.52; 935/23, 24, 27, 32, 34, 44, 47, 48, 66, 70, 71 [IMAGE AVAILABLE]

15. 5,288,852, Feb. 22, 1994, Human tumor necrosis factor polypeptides; Masaaki Yamada, et al., 530/351; 424/85.1; 435/69.5, 69.7; 530/395; 930/144 [IMAGE AVAILABLE]

16. 5,262,309, Nov. 16, 1993, Terminal modifications of tumor necrosis factor; Satoshi Nakamura, et al., 435/69.5, 172.3; 530/351 [IMAGE AVAILABLE]

17. 5,256,568, Oct. 26, 1993, Vectors and transformed most cells for recombinant protein production with reduced expression of selectable markers; Nikos Panayotatos, 435/252.33, 69.1, 172.1, 172.3, 252.3, 320.1; 536/24.1 [IMAGE AVAILABLE]

18. 5,247,070, Sep. 21, 1993, N-terminal muteins of tumor necrosis factor; Nobutoshi Yamada, et al., 530/351; 424/85.1; 435/69.5, 69.7; 530/395, 402; 930/144 [IMAGE AVAILABLE]

19. 5,219,759, Jun. 15, 1993, Recombinant DNA encoding PDGF A-chain polypeptide and expression vectors; Carl-Henrik Heldin, et al., 435/320.1, 69.4; 530/324, 399; 536/23.5, 23.51 [IMAGE AVAILABLE]

20. 5,219,727, Jun. 15, 1993, Quantitation of nucleic acids using the polymerase chain reaction; Alice M. Wang, et al., 435/6, 91.2, 91.21; 536/24.33; 935/77, 78 [IMAGE AVAILABLE]

21. 5,182,196, Jan. 26, 1993, Expression systems for overproduction of desired proteins; Bernard Allet, et al., 435/69.5, 252.3; 536/23.5, 23.51 [IMAGE AVAILABLE]

22. 5,180,811, Jan. 19, 1993, Proteins having a TNF action comprising TNF-fibronectin fusion protein; Thomas Doerper, et al., 530/351; 424/85.1; 435/69.52, 69.7; 530/395; 930/144 [IMAGE AVAILABLE]

23. 5,151,349, Sep. 29, 1992, Method for expressing polypeptide having anti-tumor activity; Shoji Tanaka, et al., 435/69.1 [IMAGE AVAILABLE]

24. 5,147,638, Sep. 15, 1992, Inhibition of tumor growth by blockade of the protein C system; Charles T. Esmon, et al., 424/85.1, 85.2, 85.4, 85.5, 152.1, 172.1, 282.1; 435/212; 514/2, 8, 12; 530/351, 381, 388.25, 389.3 [IMAGE AVAILABLE]

25. 5,136,021, Aug. 4, 1992, TNF-inhibitory protein and a method of production; Wlodzimierz E. Dembinski, et al., 530/350, 351, 369 [IMAGE AVAILABLE]

26. 5,081,021, Jan. 14, 1992, DNA encoding HTNF variants exhibiting enhanced activity; Den'ichi Mizuno, et al., 435/69.5, 91.41, 320.1; 536/23.1, 23.5; 935/9, 11, 12, 13 [IMAGE AVAILABLE]

27. 5,043,271, Aug. 27, 1991, DNA encoding rabbit TNE, vector having said DNA inserted thereinto, host transformed with said vector, rabbit TNF polypeptide, and process for production thereof; Masaaki Yamada, et al., 435/69.5, 91.41, 172.3, 240.1, 240.2, 240.4, 252.3, 252.33, 320.1; 536/23.51, 24.1; 935/2, 11, 21, 27, 60, 73 [IMAGE AVAILABLE]

28. 5,028,420, Jul. 2, 1991, Muteins of tumor necrosis factor; Tsukio Masegi, et al., 424/85.1; 435/69.5, 320.1; 530/351 [IMAGE AVAILABLE]

29. 4,990,455, Feb. 5, 1991, Novel human TNF polypeptide mutants and DNA's encoding said mutants; Junichi Yamagishi, et al., 435/69.5, 69.1, 172.3, 252.3, 252.33, 320.1; 530/350, 351; 536/23.2, 23.5; 935/10 [IMAGE AVAILABLE]

30. 4,948,875, Aug. 14, 1990, Novel polypeptide having an anti-tumor activity and a method of preparation thereof; Shoji Tanaka, et al., 530/350; 435/69.1, 69.5; 530/351 [IMAGE AVAILABLE]

31. 4,880,915, Nov. 14, 1989, Method for purifying a physiologically active substance produced by recombinant DNA technique; Junichi Kajihara, et al., 530/413; 435/69.5; 530/350, 351, 415, 416, 828 [IMAGE AVAILABLE]

32. 4,879,226, Nov. 7, 1989, Novel human physiologically active polypeptide; Robert B. Wallace, et al., 435/68.1, 172.3, 240.2, 252.33, 254.2, 320.1, 948; 514/2, 12, 21; 530/350, 351, 828; 536/23.2, 23.5; 935/9, 11, 56, 73 [IMAGE AVAILABLE]

33. 4,650,674, Mar. 17, 1987, Synergistic cytotoxic composition; Bharat B. Aggarwal, et al., 424/85.5, 85.4; 435/69.5; 514/12; 930/143, 144 [IMAGE AVAILABLE]

=> d L6 1-

1. 5,578,444, Nov. 26, 1996, Sequence-directed DNA-binding molecules compositions and methods; Cynthia A. Edwards, et al., 435/6, 7.23; 536/23.1; 935/76, 77 [IMAGE AVAILABLE]
2. 5,519,000, May 21, 1996, Tumor necrosis factor inhibitors; George A. Heavner, et al., 514/12, 13, 14, 15, 16, 17, 18; 530/324, 326, 328, 329, 330 [IMAGE AVAILABLE]
3. 5,506,340, Apr. 9, 1996, Tumor necrosis factor inhibitors; George A. Heavner, 530/324, 325, 326, 327, 328, 329, 330 [IMAGE AVAILABLE]
4. 5,486,595, Jan. 23, 1996, Tumor necrosis factor inhibitors; George A. Heavner, 530/324, 325, 326, 327, 328, 329, 330 [IMAGE AVAILABLE]
5. 5,457,129, Oct. 10, 1995, Inhibition of nitric oxide production by retinoic acid; Bharat B. Aggarwal, et al., 514/557, 825, 895, 903 [IMAGE AVAILABLE]
6. 5,455,240, Oct. 3, 1995, Modulators of pneumococcal adhesion to cellular targets involving the platelet activating factor receptor, and uses thereof; Elaine I. Tuomanen, et al., 514/210; 424/122; 514/8, 25; 536/4.1, 17.4, 17.6, 21 [IMAGE AVAILABLE]
7. 5,451,518, Sep. 19, 1995, Purified human ceramide-activated protein kinase; Richard N. Kolesnick, 435/194; 424/94.5; 435/15 [IMAGE AVAILABLE]
8. 5,447,851, Sep. 5, 1995, DNA encoding a chimeric polypeptide comprising the extracellular domain of TNF receptor fused to IgG, vectors, and host cells; Bruce A. Beutler, et al., 435/69.7, 69.5, 240.2, 320.1; 530/300, 351; 536/23.4 [IMAGE AVAILABLE]
9. 5,422,120, Jun. 6, 1995, Heterovesicular liposomes; Sinil Kim, 424/450; 264/4.1, 4.3, 4.6; 436/829 [IMAGE AVAILABLE]
10. 5,227,368, Jul. 13, 1993, Endotoxin-induced thrombosis factor which induces procoagulant activity in endothelial cells; Herwig Gerlach, et al., 514/12; 530/324, 350, 351 [IMAGE AVAILABLE]
11. 5,225,212, Jul. 6, 1993, Microreservoir liposome composition and method; Francis J. Martin, et al., 424/450, 78.31, 426 [IMAGE AVAILABLE]
12. 5,136,021, Aug. 4, 1992, TNF-inhibitory protein and a method of production; Wlodzimierz E. Dembinski, et al., 530/350, 351, 369 [IMAGE AVAILABLE]
13. 5,071,872, Dec. 10, 1991, Method for improving interleukin-2 activity using aci-reductone compounds; Donald T. Witiak, et al., 514/473; 424/85.4, 85.7; 514/465, 889; 530/351 [IMAGE AVAILABLE]

AN - 91-081851/12
 XRAM- C91-034797
 TI - Insoluble tumour necrosis factor binding proteins - and DNA encoding them, useful in pharmaceutical prods. and for antibody prodn.
 DC - B04 D16
 PA - (HOFF) HOFFMANN-LA ROCHE AG
 IN - BROCKHAUS M, DEMBIC Z, GENTZ R, LESSLAUER W, LOTSCHER H, SCHLAEGER EJ NP - 1
 PN - EP-417563-A 91.03.20 (9112)
 LA - G
 DS - AT BE CH DE DK FR GB IT LI NL
 CT - (G)No-SR.Pub
 PR - 90.04.20 90CH-001347 89.09.12 89CH-003319 90.03.08 90CH-000746
 AP - 90.08.31 90EP-116707
 IC - A61K-039/39 C07K-003/28 C07K-015/12 C12N-001/21 C12N-015/12
 AB - (EP-417563)

Insoluble TNF-BPs, or soluble and insoluble fragments of these (55 or 75 kD SDS PAGE), in homogeneous form, and their salts are new. DNA sequence (I) encoding TNF-BPs, and derived amino acid sequences are given in the specification. (I) consists of a sequence encoding a TNF-BP and a sequence encoding all domains, except the first domain, of the human Ig having chain constant region (IgG, IgA, IgM, IgE, esp. IgM, IgG, type 1 or 3). TNF-BP can be prepared by culturing hosts, e.g. mammalian or insect cells, transformed with a vector containing (I), and isolating and purifying the product.

USE/ADVANTAGE - TNF-BP is used in a therapeutic product, and as a antigen for the production of mono- and polyclonal antibodies.

In an example specific TNF-binding capacity at various concns. is measured in a filter test: $K_d = 10^{-9} - 10^{-10}$ M. (26pp Dwg.No.0/4)

**This Page is Inserted by IFW Indexing and Scanning
Operations and is not part of the Official Record**

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☐ BLACK BORDERS
- ☒ IMAGE CUT OFF AT TOP, BOTTOM OR SIDES
- ☐ FADED TEXT OR DRAWING
- ☐ BLURRED OR ILLEGIBLE TEXT OR DRAWING
- ☐ SKEWED/SLANTED IMAGES
- ☐ COLOR OR BLACK AND WHITE PHOTOGRAPHS
- ☐ GRAY SCALE DOCUMENTS
- ☐ LINES OR MARKS ON ORIGINAL DOCUMENT
- ☐ REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY
- ☐ OTHER: _____

IMAGES ARE BEST AVAILABLE COPY.

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.